Title

Depressive symptoms in adolescents with CFS: Are rates higher than in controls and do depressive symptoms affect outcome?

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Conflicts of Interest

TC is the author of several self-help books on chronic fatigue for which she has received royalties. KR has co-authored a book with TC called "Overcoming Chronic Fatigue in Young People". ML and SA declare that they have no conflicts of interest.

Abstract

Previous research has indicated that co-morbid depression is common in adolescents with Chronic Fatigue Syndrome (CFS).

Objectives: We sought to compare the characteristics of depressive symptoms in adolescents with CFS to those of healthy controls and illness controls (adolescents with asthma).

Design: Case control study nested within a prospective clinical cohort.

Methods: 121 adolescents with CFS who attended an initial assessment at two specialist CFS units completed the Children's Depression Inventory. Their responses were compared to 80 healthy controls and 27 adolescents with asthma (illness controls). The clinical cohort of adolescents with CFS completed questionnaires at assessment, and those who were seen subsequently for treatment at the CFS unit (68%), completed the measures again at their first treatment session.

Results: CFS participants scored significantly higher on all the depression subscales than participants with asthma and healthy controls. Depression score explained 11% of the variance in subsequent fatigue, but only 1.9% of the variance in physical functioning. Depression score also explained most (68%) of the variance in subsequent depression.

Conclusion: Depressive symptoms are more prominent in adolescents with CFS than in healthy controls or illness controls. Depressive symptoms also appear to remain over time during a naturalistic follow-up where no treatment was provided. This highlights the need for further research into depression in CFS, including stratifying treatment outcomes by depression status to determine what is effective at addressing these symptoms.

Keywords: depression, adolescents, CFS, fatigue, comorbidity

Introduction

Chronic Fatigue Syndrome (CFS) affects between 0.1 and 2% of adolescents (Brigden, Loades, Abbott, Bond-Kendall, & Crawley, 2017). A diagnosis of CFS is made when an adolescent experiences

severe, disabling and unremitting fatigue, lasting for ≥ 3 months, in the absence of another medical explanation for it (NICE, 2007). They may experience other symptoms, including pain, headaches, nausea, dizziness and problems with attention and concentration (NICE, 2007). Depression seems to be particularly prevalent in adolescents with CFS, with as many as one in three experiencing elevated depressive symptoms (Bould, Collin, Lewis, Rimes, & Crawley, 2013; Bould, Lewis, Emond, & Crawley, 2011; Walford, Nelson, & McCluskey, 1993) or meeting a diagnosis of depression (Garralda & Rangel, 2004, 2005; Loades, Rimes, Ali, Lievesley, & Chalder, 2017).

Depression is characterised by low mood, often accompanied by a lack of enjoyment in activities (anhedonia), as well as affective, cognitive and physiological symptoms (A.P.A., 2013). To meet a diagnosis of major depressive disorder (MDD) on the DSM-5 (A.P.A., 2013), an individual is required to have 5 of 9 symptoms, including at least one of the core symptoms of low mood, irritable mood or anhedonia, as well as a number of the additional symptoms such as insomnia/hypersomnia, changes in appetite, feelings of guilt or worthlessness and psychomotor retardation/agitation. The diagnostic criteria specify that these symptoms need to be impacting significantly on the person's functioning. Therefore, MDD is a heterogeneous disorder and the clinical presentation of depression may differ from person to person.

The most effective treatment currently available for CFS in adolescents is Cognitive Behaviour Therapy (CBT), but a considerable minority of adolescents do not recover, even with treatment (Lloyd, Chalder, & Rimes, 2012; Nijhof, Bleijenberg, Uiterwaal, Kimpen, & van de Putte, 2012). CBT for CFS entails engaging in making behavioural changes by stabilising and then gradually increasing levels of activity, alongside cognitive work to challenge unhelpful thoughts about fatigue and other concomitant symptoms, whilst building self-efficacy and shifting the focus of attention away from fatigue (Nijhof, Bleijenberg, Uiterwaal, Kimpen, & van de Putte, 2011). The cognitive model of depression purports that people with depression tend to have a negative view of the self, the world

and the future, and to think that they are helpless and to view the future in pessimistic terms (Beck, 1979). They may also lack motivation. Such characteristics of depression may impact on their ability to engage in treatment. Therefore, it is possible that those adolescents who have raised depression symptoms, as a result of feeling more helpless, hopeless and lacking motivation, are less likely to be able to make and sustain the behavioural and cognitive changes required in CBT for CFS. This may mean that they are less likely to recover from CFS. CBT is an evidence-based treatment for depression in adolescents (Goodyer et al., 2016; NICE, 2015), although the sequence in which change techniques are applied, and the specific focus and content of these techniques may be different from that in CBT for CFS (Loades & Chalder, 2017). Understanding more about depression in adolescents with CFS, including the characteristics of the depressive symptoms and the impact these have on outcome could aid our understanding of the maintenance of CFS and of potential moderators of outcome.

The aim of the current study was to explore depressive symptoms in adolescents with CFS compared to an illness controls (adolescents with asthma) and healthy controls, and to investigate the impact of depressive symptoms on outcome in CFS.

The hypotheses were:

1) Rates of depressive symptoms will be higher in CFS participants compared to persons with asthma and HCs.
2) Those adolescents with CFS who have elevated depressive symptoms at baseline will have less favourable outcomes on fatigue, functioning and subsequent depression at follow-up.

Method:

Participants

We recruited 3 groups of participants, who completed questionnaires at baseline. The eligibility criterion for all 3 groups was adolescents, age 11-18.

CFS participants: The additional eligibility criterion for this group was a clinician confirmed diagnosis of CFS (NICE, 2007). By definition, those with a primary psychiatric disorder do not meet the diagnostic criteria for CFS and are therefore excluded from this group. In total, 207 adolescents attended an assessment, of whom 135 were eligible to participate. One hundred and twenty one (89.6%) took part (see Table 1 for participant demographics).

Asthma participants: The additional eligibility criteria for this group was being prescribed medication for asthma, and having no history of psychiatric disorder.

Healthy controls: The additional eligibility criteria were no history of CFS, asthma, or psychiatric disorder.

[insert table 1 about here]

Measures

Adolescents completed the following measures (see Table 2 for reliability analysis):

Depression – the Children's Depression Inventory, CDI (Kovacs, 1992) is a self-report measure which contains 27 items. The recall period is the last two weeks, and each item is rated on a 3 point scale. The CDI is composed of 5 subscales, which are based on the empirically derived factors of negative mood, ineffectiveness, anhedonia, low self-esteem and interpersonal problems. A total score for all 27 items can also be calculated. Both the subscales and the total score were utilised in the analysis. Higher scores indicate more depressive symptoms. It is reliable and valid (Kovacs, 1992).

Anxiety – the State Trait Anxiety Inventory, STAI (Speilberger, Gorsuch, & Lushene, 1970) is a self-report measure, composed of 40 items, 20 of which relate to general threat sensitivity, or 'trait anxiety', and 20 of which relate to anxiety in response to particular threats, or 'state anxiety'. The trait anxiety items are rated with reference to how the person feels generally, and the state anxiety items with reference to how the person feels right at the moment when they are completing the measure. Each item is rated on a 4 point scale, and the subscale scores are calculated by summing the scores for the relevant items. Higher scores indicate higher anxiety levels. Valid and reliability have been established previously (Speilberger et al., 1970).

Fatigue – the 11-item Chalder Fatigue Questionnaire, CFQ (Chalder et al., 1993) assesses fatigue severity over the past month, encompassing both physical and mental fatigue. Each item is rated on a 4 point scale. The Likert method of scoring was used, resulting in a possible maximum score of 33. Higher scores indicate higher levels of fatigue. The CFQ has established reliability and validity (M Cella & Chalder, 2010).

Physical Functioning – the self-report Short Form 36 physical functioning subscale, SF36PFS (Ware & Sherbourne, 1992) has 10 items, which assess the extent to which a respondent is limited by their health across a range of activities of daily living. Each item is rated on a 3 point scale (scored 0, 5, or 10), with a possible maximum score of 100, calculated by summing the scores on each item. Higher scores indicate better physical functioning. The SF36 has been previously validated in adolescent chronic illness samples e.g. cystic fibrosis (Gee, Abbott, Conway, Etherington, & Webb, 2002).

School and social adjustment – the Work and Social Adjustment Scale (Mundt, Marks, Shear, & Greist, 2002) has 5 items which ask about functioning in work, domestic, social and leisure activities and close relationships. Each item is rated on a 9 point scale (scored 0-8). The total possible score is 40, calculated by summing the scores across individual items, with higher scores indicating more

impairment. It has established psychometric properties in CFS patients (Matteo Cella, Sharpe, & Chalder, 2011). 'School/college' was substituted for 'work' in this study.

[insert table 2 about here]

Procedure

CFS patients: A pack of questionnaires and an invitation letter, describing the potential uses of the data for research and evaluation, were sent to all those invited to attend an initial assessment appointment at 2 specialist CFS units. At the initial assessment, the healthcare professional provided the person with an information sheet, sought their consent to participate and collected the completed questionnaires. Of the CFS group, 82 (67.8%) participants completed questionnaires again at the first treatment appointment attended (although some did not attend this treatment appointment due to funding issues, or because they did not require treatment). The interval between time 1 (initial assessment) and time 2 (follow-up pre-treatment) was, on average, 3.3 months (S.D. 2.05, range 0.89-13.60).

[insert table 3 about here]

Asthma patients: Persons who met the inclusion criteria were identified by GP surgeries, who posted them an invitation letter and research pack. Baseline measures only were administered to this group.

Healthy controls: Potential participants were identified through secondary schools, who sent a letter inviting them to participate, and a research pack. The relatives of clinic staff were also invited to participate, providing they met the eligibility criteria. Baseline measures only were administered to this group.

Ethical Approval

NHS research ethics committee (LREC, ref 08/H0807/107) and the relevant research and development department approval was obtained. Furthermore, the local NHS clinical audit committee approved the collection and analysis of routine outcomes.

Data Analysis Plan

SPSS 24.0 was used to conduct the analysis. On any particular scale, where < 25% of the data for a participant was missing, the mean of the completed items was substituted in place of the missing value(s).

Power and Sample Size: G Power 3.0 was used to calculate sample size required to detect an effect. Comparing two independent means, α (sig level) of 0.05 and power of 0.9, 34 participants per group would be required to detect a large effect (d = 0.8) with two-tailed tests, and 28 participants per group with one tailed tests.

One-way ANOVAs were used to compare the groups on demographic and the variables of interest, with post-hoc pairwise comparisons with Bonferroni correction conducted to establish the direction of significant findings. As the aim of the current study was to explore possible group differences in depression symptoms, we opted not to adjust for multiple testing as this would be overly conservative in the context of a preliminary study.

A hierarchical linear regression, informed by the results of the correlations and by theoretical assumptions based on previous studies, was used to look at predictors of change over the follow-up period in the CFS participants for whom follow-up data was available. Fatigue (CFQ), functioning (SF36PFS) and subsequent depression (CDI) were the outcomes of interest.

Fatigue/functioning/depression, at baseline and time elapsed between the baseline and the follow-up, were included as covariates.

Results

A one-way ANOVA was conducted to compare groups. The groups did not differ significantly on mean age but did differ on fatigue, functioning, anxiety and depression (table 3). As predicted, participants with CFS scored significantly higher on the CDI than participants with asthma and healthy controls. This held true across all 5 CDI subscales.

Those CFS participants followed-up did not differ significantly from those who were not followed up (see Table 4), although there was a non-significant trend for those who were followed-up to be functioning better at school/socially (SSAS), and to be higher in state anxiety (STAI-S).

[insert tables 3 and 4 about here]

A hierarchical linear regression in which fatigue at time 2 was the outcome of interest was conducted. The following variables were entered into the model as covariates: time elapsed between time 1 and time 2 (time interval), baseline fatigue, and depression. The results showed that a larger time interval and baseline fatigue accounted for 32.8% of the variance in fatigue at time 2. Baseline CDI score explained a further 11.2% of the variance (see table 5). For physical functioning at time 2, a larger time interval and baseline physical functioning explained 64.7% of the variance. Only a further 1.9% was explained by CDI score (see table 5). For depressive symptoms at time 2, time interval explained 2.7% of the variance, with baseline CDI score explaining a further 68.3% (see table 5).

[insert table 5 about here]

Discussion

Adolescents with CFS had more depressive symptoms than adolescents with asthma and healthy controls, including higher levels of negative mood, ineffectiveness, anhedonia, low self-esteem and interpersonal problems. In the CFS participants, depressive symptoms at time 1 accounted for some of the variance in fatigue at time 2, but did not explain much of the variance in subsequent physical functioning. Depressive symptoms at time 1 explained most of the variance in subsequent depressive symptoms.

Notably, the mean depression score on the CDI in the CFS participants in this study was close to recommended cut-offs for identifying depression (Roelofs et al., 2010), suggesting that more than one third (45/121) of the sample scored at or above the cut-off of > 16 (Roelofs et al., 2010) for depression. This is slightly higher than existing studies, which indicate a prevalence rate of around 30% (Bould et al., 2013; Garralda & Rangel, 2004, 2005; Loades et al., 2017; Walford et al., 1993). It may be that the CDI is better used as a continuous measure of depression rather than a diagnostic instrument per se (Matthey & Petrovski, 2002). No normative data is available for the CDI in fatigued samples specifically, and given that symptoms of CFS and depression overlap, different cut-off scores may be needed (Loades et al., 2017). In the current study, approximately 5% (4/78) of the healthy controls and 15% (4/27) of the asthma controls scored above the cut-off for depression. For the healthy controls, this is comparable to the expected point prevalence of depression in adolescents, which ranges from 3 – 8% (Brent & Maalouf, 2015). Rates of depression in the asthma sample were somewhat raised compared to healthy controls but were considerably lower than those in the CFS sample.

Several explanations for the connection between CFS and depression in adolescents are possible. First, a biological mechanism may explain the high rates of depression in adolescents with CFS; the

prevalence of depression in the general population rises substantially in adolescence (Merikangas, Nakamura, & Kessler, 2009), as do rates of CFS (Crawley, 2013). It is possible that there is a subtype of CFS that is particularly associated with co-morbid depression (Williams, Chalder, Sharpe, & White, 2017). It follows that fatigue and depression are potentially linked at a biological level (Lamers, Hickie, & Merikangas, 2013). A second potential explanation for the overlap is behavioural; adolescents with CFS have to give up doing things that they enjoy as a result of their illness (Taylor, Loades, Brigden, Collin, & Crawley, 2017), which may result in a lack of positive reinforcement, resulting in depressive symptoms. Those who are particularly fatigued may have to give up more of their activities, compounding this effect. A third possibility is that significant fatigue could result from depression, given that fatigue is a symptom of depression (A.P.A., 2013). Longitudinal data in a prospective community sample has shown that depression can predict subsequent fatigue (Rimes et al., 2007).

Depressive symptoms at the time of presenting to the specialist unit were highly predictive of subsequent depressive symptoms. No treatment was systematically offered during this follow-up period. It appears that depressive symptoms are likely to require treatment, and do not appear to remit spontaneously in adolescents with CFS. However, this data must be interpreted with caution as the control groups were not followed up, so it is not clear whether this pattern is specific to CFS or extends to adolescents more broadly. We also did not control for factors such as age, gender, pain, weight and health-related quality of life; therefore, it is possible that our findings over-estimate the impact of depressive symptoms. The current findings suggest that depressive symptoms play a part in predicting fatigue outcomes longitudinally.

To further explore the effects of depression in CFS, future studies might assess cognitions such as negative thinking errors and self-esteem. Importantly, previous treatment trials in CFS have not been sufficiently powered to detect treatment effects in those with co-morbid depression, so further

research is needed to determine the effectiveness of treatment approaches for the group of adolescents who have both CFS and co-morbid depression (Loades, Sheils, & Crawley, 2016). It may be particularly important to target low mood using treatment approaches such as behavioural activation, which aims to gradually reintroduce pleasurable activities. There is an emerging evidence base for behavioural activation in adolescents with depression (Pass, Lejuez, & Reynolds, 2017).

A thorough assessment of mental health at the time of a CFS diagnosis is important to enable any co-morbid distress and co-morbidities to be identified and managed in a timely manner (Loades & Chalder, 2017; Loades et al., 2017). As a tool to aid diagnostic assessment, validated measures with established cut-off points are required.

Strengths and Limitations

Participants were consecutively recruited from specialist CFS units, although this setting does limit the generalisability of the findings to those presenting to specialist services. The asthma control group may also be a biased comparison sample due to the recruitment method, and because despite having a chronic illness, they may be relatively well and free of symptoms if their asthma is well-managed. We did not include a measure of illness impact or health related quality of life, which future studies could do. The ethnic origin of the CFS participants and the predominance of females (as would be expected from the epidemiology of CFS, Crawley (2014) was different to that of the control groups.

In the current study, the CDI was used as a proxy for a confirmed clinical diagnosis of depression. However, the CDI has not been psychometrically examined in fatigued samples, nor specifically validated for use in adolescents with CFS. Therefore, the assumption that it is a valid and reliable measure of depression may be questionable, given the overlap between symptoms of CFS and

depression (e.g. fatigue, lack of energy, sleep problems). The follow-up period was variable, although we controlled for this in the analysis.

Conclusion

This study found that adolescents with CFS endorsed more depressive symptoms on all subscales of the Children's Depression Inventory than adolescents with asthma and healthy controls did. This included higher levels of negative mood, ineffectiveness, anhedonia, low self-esteem and interpersonal problems. In the CFS group, depressive symptoms persisted over time as well. Changes in depressive symptoms may account for some of the persistence of fatigue over time but did not appear to explain changes in physical functioning.

Table 1. Participant demographics

	CFS participants (n=121)	Asthma participants (n=27)	Healthy Controls (n=78)
Age (mean)	15.0	14.9	14.6
		Gender – N (%)	
Males	35 (28.9)	12 (44.4)	30 (38.5)
Females	86 (71.1)	15 (55.6)	48 (61.5)
		Ethnicity – N(%)	
White British	86 (71.1)	16 (59.3)	65 (83.3)
Black British	2 (1.7)	1 (3.7)	1 (1.3)
Asian/British Asian	3 (2.5)	2 (7.4)	2 (2.6)
Other British/ European/White	25 (20.7)	7 (25.9)	
Other Black/Asian			4 (5.2)
Mixed race	4 (3.3)		2 (2.6)
Not stated	4 (3.3)	1 (3.7)	4 (5.1)

Table 2. Reliability Analysis (Cronbach's alpha) for measures

Measure/Subscale	CFS	Asthma	HC
CFQ	0.89	0.66	0.82
SF36PFS	0.91	0.72	0.90
SSAS	0.81	0.76	0.83
CDI	0.90	0.85	0.84
STAI-S	0.93	0.92	0.94
STAI-T	0.92	0.94	0.93

CDI – Children's Depression Inventory, CFQ – Chalder Fatigue Questionnaire, SSAS – School and Social Adjustment Scale, SF36PFS – Short form 36 physical functioning subscale, STAI –State-Trait Anxiety Inventory

Table 3. Between group comparison on baseline variables

	Group				
	CFS	**Asthma**	**Healthy controls**	**Group difference**	**Direction of group differences established in post-hoc tests**
	Mean (SD)	**Mean (SD)**	**Mean (SD)**		
Age (years)	15.0 (1.7)	15.0 (2.2)	14.6 (1.4)	*F*(2,223)= 1.57, *p*=.210	
Fatigue (CFQ)	23.2(5.8)	11.9 (2.7)	10.5 (3.8)	*F*(2,222)= 182.09, *p*<.0001	
Physical functioning (SF36PFS)	50.0 (25.1)	88.5 (12.7)	90.3 (17.1)	*F*(2, 214)= 95.23, *p*<.0001	
School and social functioning (SSAS)	24.6 (8.1)	1.9 (3.7)	1.1 (3.1)	*F*(2, 219) =370.31, *p*<.0001	
Depressive symptoms (CDI total)	15.7 (8.5)	7.3 (5.8)	5.6 (5.2)	*F*(2, 219) =50.73, *p*<.0001	CFS>asthma=HCs
CDI Negative Mood subscale	3.5 (2.7)	1.9 (1.8)	1.4 (1.6)	*F*(2, 220)= 21.62, *p*<.0001	CFS>asthma=HCs
CDI Interpersonal Problems subscale	0.8 (1.0)	0.3 (0.5)	0.6 (0.9)	*F*(2, 220)= 13.88, *p*<.0001	CFS>asthma=HCs
CDI Ineffectiveness subscale	3.0 (2.0)	1.4 (1.4)	1.1 (1.4)	*F*(2, 213)= 28.29, *p*<.0001	CFS>asthma=HCs
CDI Anhedonia subscale	6.4 (2.9)	2.2 (2.1)	1.8 (1.9)	*F*(2, 220)= 89.51, *p*<.0001	CFS>asthma=HCs
CDI Negative Self-esteem subscale	2.1 (2.0)	1.5 (1.3)	1.1 (1.2)	*F*(2, 220)= 9.12, *p*<.0001	CFS>asthma=HCs

State Anxiety (STAI-State)	45.5 (12.6)	34.8 (10.4)	34.8 (11.4)	$F(2, 222) = 22.51$, $p < .0001$	CFS>asthma=HCs
Trait Anxiety (STAI- Trait)	48.0 (11.6)	39.7 (11.4)	37.5 (11.2)	$F(2, 222) = 21.71$, $p < .0001$	CFS>asthma=HCs

CDI – Children's Depression Inventory, CFQ – Chalder Fatigue Questionnaire, SF36PFS – Short Form 36 Physical Functioning Subscale, SSAS – School and Social Adjustment Scale, STAI – State-Trait Anxiety Inventory

Table 4. Comparison of means between CFS participants with 2 data points and those only seen once

	CFS mean (S.D.) – 2 data points	CFS mean (S.D.) – 1 data point	Significance Tests – t (df)	Significance level (p)	Mean difference (95% CI)	S.E. of mean difference
Age	14.94 (1.77)	15.15 (1.57)	-0.65 (119)	.520	-0.22 (-0.44-0.87)	0.33
CFQ	23.17 (5.89)	23.26 (5.60)	0.09 (118)	.932	0.10 (-2.16-2.35)	1.14
SSAS	23.73 (7.88)	26.45 (8.37)	1.73 (117)	.086	2.72 (-0.39-5.83)	1.57
SF-36PFS	51.64 (24.69)	46.25 (25.94)	-1.06 (111)	.294	-5.38 (-15.50-4.73)	5.10
CDI Total	16.38 (8.84)	14.29 (7.56)	-1.24 (115)	.217	-2.09 (-5.42-1.24)	1.68
CDI Negative Mood subscale	3.78 (2.76)	3.06 (2.58)	-1.35 (116)	.181	-0.72 (-1.77-0.34)	0.53
CDI Interpersonal Problems subscale	0.88 (1.01)	0.77 (1.03)	-0.54 (116)	.594	-0.11 (-0.50-0.29)	0.20
CDI Ineffectiveness subscale	3.08 (2.07)	2.74 (1.95)	-0.81 (116)	.420	-0.34 (-1.16-0.49)	0.42
CDI Anhedonia subscale	6.39 (2.83)	6.26 (3.03)	-0.22 (116)	.825	-0.13 (-1.26-1.00)	0.57
CDI Negative Self-esteem subscale	2.21 (2.06)	1.83 (1.82)	-0.97 (116)	.337	-0.38 (-1.15-0.40)	0.39
STAI-S	46.95 (11.92)	42.37 (13.56)	-1.87 (118)	.063	-4.58 (-9.42-0.26)	2.44
STAI-T	48.71 (11.73)	46.57 (11.42)	-0.94 (118)	.352	-2.14 (-6.66-2.39)	2.28

2-tailed tests

CDI – Children's Depression Inventory, CFQ – Chalder Fatigue Questionnaire, SF36 – Short for 36 physical functioning subscale, SSAS – School and Social Adjustment Scale, STAI – State-Trait Anxiety Inventory

Table 5. Hierarchical linear model of predictors of outcome at time 2

	Unstandardised B	**S.E. *B***	**Standardised *B***	**T**	***P***
			Outcome: Time 2 Fatigue		
Step 1					
Constant	8.33	2.88		2.89	.005
Time between T1 & T2	-0.25	0.35	-0.08	-0.73	.471
T1 fatigue	0.64	0.12	0.57	5.45	<.000
r^2 = 0.328, p < .000					
Step 2					
Constant	8.38	2.65		3.17	.002
Time between T1 & T2	-0.52	0.33	-0.16	-1.57	.121
T1 fatigue	0.47	0.12	0.43	4.02	<.000
T1 CDI	0.28	0.08	0.38	3.46	.001
r^2 = 0.439, r^2 change = 0.112, p = .001					
			Outcome: Time 2 Physical Functioning (SF36PFS)		
Step 1					
Constant	3.35	6.10		0.55	.585
Time between T1 &T2	1.96	0.97	0.16	2.03	.047
T1 SF36PFS	0.86	0.08	0.81	10.34	<.000
r^2 = 0.647, p < .000					
Step 2					
Constant	10.20	7.06		1.45	.154
Time between T1 &T2	2.36	0.97	0.19	2.42	.018
T1 SF36PFS	0.83	0.08	0.78	10.08	<.000
T1 CDI	-0.43	0.23	-0.15	-1.83	.073
r^2 = 0.666, r^2 change = 0.019, p = .073					
			Outcome: Time 2 Depressive symptoms (CDI)		
Step 1					
Constant	13.53	2.19		6.19	.000
Time between T1 & T2	0.71	0.55	0.16	1.28	.206
r^2 = 0.027, p < .206					
Step 2					
Constant	3.03	1.50		2.02	.048
Time between T1 & T2	-0.37	0.32	-0.09	-1.15	.254
T1 CDI	0.89	0.08	0.86	11.69	<.000
r^2 = 0.710, r^2 change = 0.700, p < .000					

B = Beta, CBRQ - Cognitive and Behavioural Responses Questionnaire, CDI – Children's Depression Inventory, CFQ – Chalder Fatigue Questionnaire, SE*B* – *Standard error of Beta,* SF36PFS – Short Form 36 Physical Functioning Subscale, STAI – State-Trait Anxiety Inventory, SSAS – School and Social Adjustment Scale, T1 – Time 1 (initial assessment), T2 – Time 2 (follow-up pre-treatment)

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